REMARKS

Reconsideration and withdrawal of the rejections to the application are respectfully requested in view of the remarks herewith.

I. THE ART REJECTIONS ARE OVERCOME

Claims 96-97 and 99-116 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Quelle *et al.* with evidence provided by Dorland's Illustrated Medical Dictionary and claims 96-116 were rejected under 35 U.S.C. §103(a) as allegedly obvious over Quelle *et al.* with evidence provided by Dorland's Illustrated Medical Dictionary. The rejections are respectfully traversed and will be addressed collectively.

The previous Notice of Allowability was withdrawn, and the above rejections re-issued in response to Applicant's June 29, 2005 Amendment which sought to clarify that the claimed erythropoietin has an activity *in vivo*, and an *in vitro* activity of at least 200,000 U/mg or at least 500,000 U/mg. Applicants respectfully assert that the claims remain novel and non-obvious over the cited references as Quelle, with or without the evidence provided by Dorland, does not teach or suggest the presently claimed invention; and, Quelle, with or without the evidence provided by Dorland, does not provide any teaching, suggestion, motivation, or incentive to modify the cited document to arrive at the instant invention.

Initially, it is respectfully pointed out that for a Section 102 rejection to stand, the single prior art reference must contain all of the elements of the claimed invention, *see Lewmar Marine Inc. v. Barient Inc.*, 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987), and, the single prior art reference must contain an enabling disclosure, *see Chester v. Miller,* 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990). It is also well-settled that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). Further, "obvious to try" is not the standard under 35 U.S.C. §103. *In re Fine,* 5 U.S.P.Q. 2d 1596, 1599 (Fed. Cir. 1988). And, as stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification." Also, the Examiner is respectfully reminded that for the Section 103 rejection to be proper, both the suggestion of the claimed invention and the

expectation of success must be founded in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988).

The Office Action states that as Applicants have "admitted" that the claimed activity of 200,000 U/mg or at least 500,000 U/mg was obtained during *in vitro* testing, and that as erythropoiesis is an inherent activity erythropoietin, the cited references anticipate and/or render obvious the present invention. Applicants respectfully disagree.

Applicants' June 29, 2005 Amendment, and the statements accompanying such amendment, were made solely for the purpose of clarifying the record when it was determined that the claims could be more clear. The test results described in the Declaration have always demonstrated that the erythropoietin has an *in vivo* activity, **and,** that the activity described therein, namely the activity of at least 200,000 U/mg or at least 500,000 U/mg was obtained during *in vitro* testing, see for example, paragraph 4a on page 3 of the Declaration. Accordingly, the claims were amended to ensure an accurate reading thereof, namely that the EPO of the present invention has *in vivo* activity, **and** an activity of at least 200,000 U/mg or at least 500,000 U/mg.

Applying the law to the instant facts, it is respectfully submitted that the instant invention is not anticipated or made obvious by Quelle, *inter alia*, because Quelle does not contain a teaching of all of the elements of the instant claims. And, it is respectfully submitted that the instant invention is not rendered obvious by Quelle, as Quelle does not provide a teaching or suggestion of all of the elements of the instant claims, *inter alia*.

The present invention relates to, *inter alia*, a substantially pure, recombinant glycosylated erythropoietin, produced by a baculovirus expression system in cultured insect cells, wherein said erythropoietin has relative homogeneity or is purified to 95% or greater and said erythropoietin stimulates erythropoiesis and has an *in vivo* activity and an activity of at least 200,000 U/mg or of about 500,000 U/mg.

The previously pending claims were allowed on the basis that Quelle *et al.* and Wojchowski *et al.* produced an EPO in *Spodoptera frugiperda* that **was not active *in vivo***, and that none of the remaining references cited against the Applicants taught the EPO of the present invention. The present invention requires that the EPO stimulate erythropoiesis, have *in vivo* activity, and an activity of at least 200,000 U/mg or of about 500,000 U/mg. None of the cited references teach or suggest all of these requirements. Indeed, the requirement of an *in vivo*

activity alone renders the claims novel and non-obvious over over Quelle *et al.* and Wojchowski *et al.*, as neither references teaches or suggests an EPO having *in vivo* activity.

This is in contrast to the assertions in the Office Action, which merely assumes (incorrectly, in the Applicants' view) that Quelle *et al.* and Wojchowski *et al.* must necessarily have *in vivo* activity. Applicants have repeatedly demonstrated that differences between the claimed EPO and the EPO of both Quelle and Wojchowski exist, including as to glycosylation.

Indeed, Applicants have actually **quoted** from page 654 of Quelle that Quelle's erythropoietin had "little, **if any**, activity *in vivo*" in an attempt to demonstrate the even Quelle does not believe that the produced EPO has *in vivo* activity. In fact, Quelle *et al.* itself provides the reason for their lack of *in vivo* activity: a lack of sialic acid. Further, Quelle *et al.* states that sialic acid is absent from saccharide structures derived from insects, such that one of skill in the art would expect the present erythropoietin, an insect-cell derived erythropoietin, to lack *in vivo* activity due to the absence of sialic acid.. Quelle at 656.

It is well known in the art that natural human EPO having a complex highly branched glycosylation pattern terminating in sialic acid residues has the highest *in vivo* activity. And, the EPO protein with no sugar residues has the highest *in vitro* activity and essentially no *in vivo* activity. Enzymatic removal of the terminal sialic acid units in an otherwise normal human EPO destroys *in vivo*, but not *in vitro* activity. Accordingly, one of skill in the art reading Quelle *et al.* would expect that as Quelle *et al.*'s EPO lacks sialic acid, it would have no *in vivo* activity, as was stated by Quelle. It is of note that as the lack of sialic acid does not destroy *in vitro* activity, there is no inconsistency in Quelle's EPO having *in vitro* activity but not *in vivo* activity, a point that the Office Action appears to struggle with.

Furthermore, the Office Action states that the distinctiveness between the presently claimed EPO and that of the prior art is not identified. Again, Applicants disagree. Example 9 specifically states that the glycosylation of EPO is important for its biological activity. Applicants respectfully submit that differences in glycosylation between the presently claimed EPO and that of Quelle (especially as glycosylation is effected by the lack of sialic acid) account for the differences in biological activity between the two. And, Applicants again point to the previously filed declaration of Dr. Manon Cox that demonstrates the *in vivo* activity of the presently claimed EPO, which is necessarily different from that which is taught by Quelle.

Therefore, because Quelle does not contain all the elements of the presently claimed invention, and because Quelle, either alone or in combination with Wojchowski, does not provide any teaching, suggestion, motivation, or incentive to modify to allow one of skill in the art to arrive at the present invention, it is respectfully requested that the rejections under 35 U.S.C. §§ 102(b) and 103(a) be reconsidered and withdrawn.

REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, prior to issuance of any paper other than a Notice of Allowance, an interview, is respectfully requested, with the Examiner his supervisor, and, the Examiner is respectfully requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

The remarks herein place the application in condition for allowance. An early and favorable consideration of the application on the merits, and prompt issuance of a Notice of Allowance are earnestly solicited.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorney for Applicants

By: Thomas J. Kowalski by Angela M. Collison

Thomas J. Kowalski
Reg. No. 32,147
Angela M. Collison
Reg. No. 51,107
(212) 588-0800